## REMARKS

The Office Action of July 30, 2003, has been received and reviewed. Claims 17-36 are currently pending, while claims 17, 18, 27-30 and 32 have been withdrawn from consideration. Claims 19-26, 31 and 33-36 stand rejected. Claims 19, 20, 25, 31 and 35 have been amended and new claim 37 has been added as set forth herein. All amendments are made without prejudice or disclaimer. Reconsideration is respectfully requested.

### Objections to the Specification

The specification was objected to for containing sequence disclosures that were not identified by sequence identifiers. The sequence identifiers have been added as set forth herein. Withdrawal of the objections is requested.

### Rejections under 35 U.S.C. § 112, first paragraph

Written Description

Claims 19, 21, 23-25, 31 and 33-35 stand rejected under 35 U.S.C. § 112, first paragraph, as assertedly failing to comply with the written description requirement. Applicants respectfully traverse the rejection as hereinafter set forth.

Specifically, it was thought that "the claims read on a therapeutic method for treating any and all inflammatory disorder or immune disease using a gene delivery capable of targeting any aberrant cell population." (Office Action, page 4). "To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor has possession of the claimed invention." (M.P.E.P. § 2163, *citing Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 U.S.P.Q.2d 1111, 1116 (Fed. Cir. 1991)). As stated in the MPEP, "[e]ach claim must be separately analyzed and given its broadest reasonable interpretation in light of and consistent with the written description." (M.P.E.P. § 2163, *citing In re Morris*, 127 F.3d 1048, 1053-54, 44 USPQ2d 1023, 1027 (Fed. Cir. 1997)).

Although applicants do not agree that the claims lack compliance with the written description requirement, to expedite prosecution, claim 19 has been amended to recite in part "a

method of treating an inflammatory disorder in a subject, said method comprising: administering a gene delivery vehicle to the subject, said gene delivery vehicle comprising: a gene capable of expressing an apoptosis inducing agent that exhibits its effect in aberrant cells involved with or related to immune diseases; wherein said apoptosis inducing agent is the apoptosis inducing protein apoptin." When amended independent claim 19 is read in light of and consistent with the specification, one of ordinary skill in the art would conclude that the applicants had possession of the claimed invention.

For instance, the as-filed specification indicates that an apoptosis inducing agent is used "for the treatment of autoimmune diseases," which includes inflammatory disorders. (*See*, Specification as-filed, page 3, lines 23-28). The as-filed specification also discloses that the apoptosis inducing agent is delivered with a "gene delivery vehicle [that] is defined [] as any vehicle capable of delivering a gene to a cell." (*See*, *Id.* at page 4, lines 5-9). Claim 19 further recites that the apoptosis inducing agent is apoptin and as described in the as-filed specification, apoptin "does not display its activity to any significant extent in normal cells, whereas the present invention shows that it does exhibit its effect in the aberrant cells involved with or related to (auto) immune diseases." (*Id.* at page 5, lines 32-37). Thus, since the as-filed specification described the elements of claim 19, one of ordinary skill in the art would conclude that the applicants had possession of the claimed invention.

With regard to claim 21, it recites that the "gene delivery vehicle further comprises a suicide gene." The as-filed specification indicates "the invention also provides a use wherein said gene delivery vehicle further comprise a suicide gene." (*Id.* at page 4, lines 24-26).

Regarding claims 23-25, 31, and 33-35, they each include elements indicating, *inter alia*, that the gene delivery vehicle has a tropism for hematopoietic cells, fibroblast-like synoviocytes, comprises a targeting means, and wherein the targeting means is for fibroblast-like like synoviocytes, as identified in each specific claim. Support for the gene delivery vehicles having the recited elements is described in the as-filed specification at page 4, lines 7-10.

Since the as-filed specification has language supporting and describing the claim language of each of claims 19, 21, 23-25, 31 and 33-35, the written description requirement is

met. Accordingly, reconsideration and withdrawal of the written description rejections of claims 19, 21, 23-25, 31 and 33-35 are requested.

Enablement

Claims 19, 20, 21, 23-25, 31 and 33-35 stand rejected under 35 U.S.C. § 112, first paragraph, as assertedly containing subject matter which was not enabled by the specification. Applicants respectfully traverse the rejection as set forth herein.

Specifically, it was thought that "the skilled artisan cannot envision the detailed structures of gene delivery vehicle[s] having a specific targeting means encompassed by these claims, thus, one would not know how to use the invention without first carrying out undue experimentation to determine what is the proper target for a specific tissue tropism." (Office Action at page 7). However, the MPEP indicates "[a]s long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. 112 is satisfied." (M.P.E.P. § 2164.01(b), *citing In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970)).

Each of independent claims 19 and 20 is directed a method of treating an inflammatory disorder or a method a treating an immune response, respectively. Each method is directed to administering a gene delivery vehicle to a subject, wherein the gene delivery vehicle comprises a gene capable of expressing an apoptosis inducing agent, such as apoptin, that exhibits its effect in aberrant cells involved with or related to immune diseases and wherein expression of the apoptosis inducing agent induces apoptosis, thus providing the treatment.

Since the specification discloses a working example of a gene delivery vehicle having a gene that encodes an apoptosis inducing agent that is able to induce apoptosis, one of ordinary skill in the art would be able to make and use the invention of claims 19 and 20. For instance, the specification describes cells, *e.g.*, fibroblast-like synoviocytes from a patient suffering from rheumatoid arthritis, that are infected with a gene delivery vehicle, *e.g.*, AdMLPvp3 (an apoptin expressing adenoviral vector), that results in a dramatic level of cell death. (*See*, Specification, page 15, line 28 through page 16, line 32). The specification further discloses that the apoptosis inducing agent may be used to treat inflammatory disorders or immune diseases. (*See*, *Id.* at

page 3, lines 23-34). The specification also discloses that the apoptosis inducing agent exhibits its effects in aberrant cells involved with or related to immune diseases, *e.g.*, apoptosis is more activated when the rheumatoid arthritis fibroblast-like cells are serum stimulated. (*See*, *Id.* at page 16, lines 33-39).

Accordingly, one of ordinary skill in the art would be able to make and use the subject matter of claims 19 and 20 without undue experimentation.

Reconsideration and withdrawal of the enablement rejections of claims 19, 20, 21, 23-25, 31 and 33-35 are, thus, requested.

**Rejections under 35 U.S.C. § 112, second paragraph**

Claims 19-26, 31 and 33-36 stand rejected under 35 U.S.C. § 112, second paragraph, as assertedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.

Although applicants do not agree that any of the claims are vague and indefinite for lacking a recitation that relates back to the preamble to indicate that the goal of the method is resolved, claims 19 and 20 have been amended to recite that expression of the apoptin inducing agent induces apoptosis in the aberrant cells, thus treating the immune disease or the inflammatory disorder in the subject. Accordingly, amended claims 19 and 20 should be definite.

Thus, reconsideration and withdrawal of the indefiniteness rejections are requested.

**Rejections under 35 U.S.C. § 102**

Claims 19, 20 and 26

Claims 19, 20 and 26 stand rejected under 35 U.S.C. § 102(a) as assertedly being anticipated by Sata et al. Applicants respectfully traverse the rejections as hereinafter set forth.

As amended, each of independent claims 19 and 20 recite that the gene delivery vehicle comprises a gene encoding apoptin. Since Sata et al. does not disclose a gene delivery vehicle

having a gene encoding apoptin, independent claims 19 and 20 cannot be anticipated. Claim 26 is novel, at the very least, as depending from novel independent claim 19.

Reconsideration and withdrawal of the anticipation rejections of claims 19, 20 and 26 are requested.

Claims 19 and 20

Claims 19 and 20 stand rejected under 35 U.S.C. § 102(a) as assertedly being anticipated by Li et al. Applicants respectfully traverse the rejections as set forth herein.

Since Li et al. does not disclose a gene delivery vehicle having a gene that encodes apoptin as recited in claims 19 and 20, they are not anticipated.

Accordingly, reconsideration and withdrawal of the anticipation rejections of claims 19 and 20 are requested.

Claims 19, 20 and 26

Claims 19, 20 and 26 stand rejected under 35 U.S.C. § 102(b) as assertedly being anticipated by International Publication WO 97/07828. Applicants respectfully traverse the rejections as hereinafter set forth.

Amended independent claims 19 and 20 each recite that the gene delivery vehicle comprises a gene encoding apoptin. Since International Publication WO 97/07828 does not disclose a gene delivery vehicle having a gene encoding apoptin, claims 19 and 20, and claim 26 depending from claim 19, cannot be anticipated.

Accordingly, reconsideration and withdrawal of the anticipation rejections of claims 19, 20 and 26 are requested.

Claims 19, 20 and 26

Claims 19, 20 and 26 stand rejected under 35 U.S.C. § 102(b) as assertedly being anticipated by Zhang et al. Applicants respectfully traverse the rejections as set forth herein.

Zhang et al. discloses a recombinant replication-defective adenovirus carrying the FasL gene and, thus, cannot anticipate amended independent claims 19 and 20 which each recite a gene delivery vehicle having a gene encoding apoptin.

Thus, reconsideration and withdrawal of the anticipation rejections of claims 19 and 20, and claim 26 depending from claim 19, are requested.

Claims 19 and 20

Claims 19 and 20 stand rejected under 35 U.S.C. § 102(b) as assertedly being anticipated by Arai et al. Applicants respectfully traverse the rejections as hereinafter set forth.

Claims 19 and 20 are not anticipated since Arai et al. does not disclose a gene delivery vehicle comprising a gene encoding apoptin.

Reconsideration and withdrawal of the anticipation rejections of claims 19 and 20 are, thus, requested.

Claims 19, 20, 21, 26 and 36

Claims 19, 20, 21, 26 and 36 stand rejected under 35 U.S.C. § 102(e) as assertedly being anticipated by McCormick et al. Applicants respectfully traverse the rejections as set forth herein.

Each of independent claims 19 and 20 are directed to a gene delivery vehicle comprising a gene encoding apoptin. McCormick et al. discloses a method to discriminate between neoplastic and non-neoplastic cells using a recombinant adenovirus that is substantially replication deficient in non-neoplastic cells and which exhibits a partial replication phenotype in neoplastic cells. (*See*, McCormick et al., Col. 3, lines 13-34). However, McCormick et al. does not disclose a gene delivery vehicle comprising a gene encoding apoptin.

Accordingly, reconsideration and withdrawal of the anticipation rejections of independent claims 19 and 20, and claims 21, 26 and 36 depending, directly or indirectly, from novel independent claim 19 are requested.

Claims 19 and 20

Claims 19 and 20 are provisionally rejected under 35 U.S.C. § 102(e) as assertedly being anticipated by co-pending U.S. Pat. Apps. 09/733,416, 09/764,176, and 09/819,308. Applicants respectfully traverse the rejections as set forth herein.

Since the currently pending patent application properly entered the National Stage under 35 U.S.C. § 371, the above-referenced patent application has an effective filing date of January 10, 2000. (*See*, M.P.E.P. § 1893.03(b)). Thus, the currently pending patent application has an effective filing date, *i.e.*, January 10, 2000, that is earlier than each of the effective filing dates of U.S. Pat. Apps. 09/733,416 (effective filing date December 8, 2000), 09/764,176 (effective filing date January 17, 2001), and 09/819,308 (effective filing date March 27, 2001).

Accordingly, reconsideration and withdrawal of the provisional rejections of claims 19 and 20 are requested.

Claims 19 and 20

Claims 19 and 20 are rejected under 35 U.S.C. § 102(f) as assertedly not being invented by the applicants. Applicants respectfully traverse the rejections as hereinafter set forth.

Specifically, it was thought that the subject matter of pending claims 19 and 20 encompass: claims 27 and 28 of U.S. Pat. App. 09/733,416; claims 17 and 24 of U.S. Pat. App. 09/764,176; and claims 15 and 19 of U.S. Pat. App. 09/819,308.

Since applicants have established that the currently pending patent application has an earlier effective filing date than any of U.S. Pat. Apps. 09/733,416, 09/764,176, and 09/819,308, and "the examiner must presume the applicants are the proper inventors," reconsideration and withdrawal of the 35 U.S.C. § 102(f) rejections of claims 19 and 20 are requested. (M.P.E.P. § 706.02(g)).

**Rejections under 35 U.S.C. § 103**

Claims 19 and 20

Claims 19 and 20 stand rejected under 35 U.S.C. § 103(a) as assertedly being unpatentable over Sata et al. in view of Zuckermann et al. Applicants respectfully traverse the rejections as set forth herein.

A *prima facie* case of obviousness cannot be established since Sata et al. and Zuckermann et al. do not, alone or in combination, teach or suggest each and every element of independent claim 19 or 20. As amended, each of independent claims 19 and 20 are directed to methods employing a gene delivery vehicle having a gene encoding "an apoptosis inducing agent that exhibits its effects in aberrant cells involved with or related to immune diseases," wherein the apoptosis inducing agent is apoptin. Sata et al. does not teach or suggest the use of apoptin that exhibits its effects in aberrant cells involved with or related to immune diseases and, in fact, does not teach or suggest a gene delivery vehicle having a gene encoding apoptin.

The disclosure of Zuckermann et al., when combined with Sata et al., does not remedy the deficiency of Sata et al. in teaching or suggesting the use of a gene delivery vehicle having a gene encoding apoptin that exhibits its effects in aberrant cells involved with or related to immune diseases as required by claims 19 and 20. Rather, Zuckermann et al. discloses that apoptin may be used to treat prostrate cancer and benign hyperplasia, and does not teach or suggest an apoptosis inducing agent in general. (*See*, Zuckermann et al., Col. 12, lines 8-48). Thus, a *prima facie* case of obviousness cannot be established with regard to independent claim 19 or 20.

Accordingly, reconsideration and withdrawal of the obviousness rejections of claims 19 and 20 are requested.

Claims 19, 21 and 22

Claims 19, 21 and 22 stand rejected under 35 U.S.C. § 103(a) as assertedly being unpatentable over McCormick et al. in view of Bujard et al. Applicants respectfully traverse the rejections as set forth herein.

A *prima facie* case of obviousness cannot be established since McCormick et al. and Bujard et al. do not, alone or in combination, teach or suggest each and every element of independent claim 19. As amended, independent claim 19 is directed to a gene delivery vehicle having a gene encoding an apoptosis inducing agent, such as apoptin. However, neither McCormick et al. nor Bujard, alone or in combination, teach or suggest a gene delivery vehicle having a gene encoding apoptin as an apoptosis inducing agent.

Thus, reconsideration and withdrawal of the obviousness rejection of claim 19, and claims 21 and 22 depending therefrom, are requested.

**Double Patenting**

Claims 19 and 20 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as assertedly being unpatentable over: claims 22 and 25 of U.S. Pat. App. 09/403,213; claims 17 and 24 of U.S. Pat. App. 09/764,176; claims 15 and 19 of U.S. Pat. App. 09/819,308; and claims 27 and 28 of U.S. Pat. App. 09/733,416. Applicants respectfully traverse the rejections as hereinafter set forth.

Claims 19 and 20 have been amended (without prejudice or disclaimer) as set forth herein. Accordingly, applicants request reconsideration of the provisional double patenting rejections of amended claims 19 and 20, and note that if any issues of obviousness-type double patenting exist in view of the cited patent applications upon an indication of allowable subject matter, the issue will be dealt with then.

## CONCLUSION

In view of the amendments and remarks presented herein, applicants respectfully submit that the claims define patentable subject matter. If questions should remain after consideration of the foregoing, the Examiner is kindly requested to contact applicants' attorney at the address or telephone number given herein.

Respectfully submitted,

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